REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Status of Claims and Claim Amendments

After entry of the amendments set forth above, the pending claims are claims 1, 7-13, 15, 16 and 33-40.

Based upon the rejections set forth in the outstanding Office Action, it appears the Examiner has not entered the amendments previously set forth in the Examiner's Amendment dated March 4, 2011. Accordingly, these amendments are set forth herein. Specifically, claims 1, 8, 9 and 13 have been amended, and claim 14 has been cancelled, without prejudice or disclaimer.

Additionally, claim 1 has been amended to recite a drug administration period and a drug holiday period of 14 days, claim 7 has been rewritten in independent form, and claims 3-6 have been cancelled, without prejudice or disclaimer.

New claims 33-40 have been added to the application, and correspond to claims 8-13, 15 and 16, but depend upon claim 7.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 1 and 3-16 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement is rendered moot in view of the claim amendments. Specifically, claim 1 has been amended to delete "or a hydrate thereof". Thus, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 8-9 and 13-14 as being indefinite under 35 U.S.C. § 112, second paragraph is rendered moot in view of the claim amendments. Specifically, claims 8, 9 and 13 have been amended in accordance with the Examiner's suggestion, and claim 14 has been cancelled, in accordance with the Examiner's suggestion. Thus, reconsideration and withdrawal of the rejection are respectfully requested.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 3-4, 8 and 10-12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Yoshino et al. (Neurological Therapeutics).

Claims 15 and 16 are also rejected under 35 U.S.C. § 102(b) as being anticipated by Yoshino et al. as evidenced by Ikeda (WO 02/34264).

These rejections are respectfully traversed.

The Examiner takes the position that Yoshino et al. teach "a method of treating Amyotrophic Lateral Sclerosis (ALS) comprising the administration of edaravone … [with] the following dose regimen: 14 day administration and then 10 days each month on a long term basis … which means there is at least 1 day holiday period in the administration."

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants' amended independent claim 1 requires a drug administration period of 14 days and a drug holiday period of 14 days. This limitation is not expressly or inherently described in the Yoshino et al. reference. In this regard, please see the discussion provided on pages 2 and 3 of the Declaration under 37 CFR 1.132 (hereafter "Declaration") submitted herewith, which further demonstrates the distinctions between Applicants' claims and the Yoshino et al. reference.

Thus, it is clear that independent claim 1, and claims 8, 10-12, 15 and 16 which are dependent upon claim 1, are not anticipated by the Yoshino et al. reference.

The Ikeda reference is relied upon to teach symptoms which are characteristic of ALS. However, this reference fails to remedy the above discussed deficiency of the Yoshino et al. reference. Accordingly, claims 1, 8, 10-12, 15 and 16 are also not anticipated by Yoshino et al. as evidenced by Ikeda.

For the reasons provided above, reconsideration and withdrawal of the anticipation rejections are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 5-7 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yoshino et al.

Claims 13 and 14 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshino et al. in view of Ikeda.

These rejections are respectfully traversed.

The Examiner takes the position that Yoshino et al. teach all the limitations of claims 5-7, except for the specific dose regimen. The Examiner asserts that Yoshino et al. teach dose regimens like "1-14 day administration and then 10 days each month on a long term basis … which means there is at least 1 day holiday period in the administration, or 2-20 day administration (Monday through Friday) … which translates in 5 day administration (Monday through Friday) and 2 day holiday period (Saturday and Sunday)." The Examiner asserts that these dose regimens are very close and/or overlap with the dose regimens of claims 5-7.

Applicants respectfully disagree with the Examiner's position.

Initially, Applicants note that claims 5, 6 and 14 have been cancelled, without prejudice or disclaimer.

The Examiner's position of obviousness is based upon *allegedly* close or overlapping ranges.

As discussed on page 2 of the Declaration submitted herewith, Yoshino et al. does not teach or suggest a dose regimen in accordance with Applicants' claims. In fact, when the drug administration of Yoshino et al. is 14 days, the drug holiday period is unknown.

Further, as discussed on pages 3 and 4 of the Declaration submitted herewith, a dosing regimen in accordance with Example 1 of the present specification (14 day drug period, followed by 14 day holiday period, followed by 10 day drug period, excluding Saturdays, Sundays and holidays) has unexpectedly superior results when compared to the dosing regimen disclosed in the Open Administration Trials of Yoshino et al. Specifically, edaravone suppressed the decline of the ALSFRS-R score for 6 months by 1.7 points in the Open Administration Trials of Yoshino

et al., while edaravone suppressed the decline of ALSFRS-R score for 6 months by 2.3 points in Example 1 of Applicants' specification. Thus, Example 1 of Applicants' specification is unexpectedly superior by 0.6 points.

As also discussed on page 4 of the Declaration, it is reported that 1 point of ALSFRS-R score increases the risk of death or tracheotomy by 7%. Thus, it is clear that the 0.6 point difference noted above is very significant for ALS patients.

MPEP 2144.05 teaches, "Applicants can rebut a *prima facie* case of obviousness based on overlapping ranges by showing the criticality of the claimed range. 'The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range.' *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)."

In this case, the Yoshino et al. reference fails to teach a dosing regimen in accordance with Applicants' amended claims. However, the Examiner has taken the position that Applicants' claims are obvious, because the claimed ranges and the prior art ranges do not overlap, but ***are close enough that one skilled in the art would have expected them to have the same properties***. (Please see the last paragraph on page 11 of the outstanding Office Action.)

However, as discussed above, the dosing regimen recited in Applicants' claims provides unexpectedly superior results when compared to the dosing regimen of the Yoshino et al. reference. Accordingly, contrary to the position of the Examiner, the ranges set forth in Applicants' claims do not have the ***same properties*** as the ranges set forth in the cited reference. Thus, Applicants have demonstrated the criticality of the recited ranges, and have thus rebutted any showing of obviousness set forth by the Examiner.

Accordingly, it is clear that the invention of claims 7 and 9 is patentable over Yoshino et al.

Regarding claims 13 and 14, the Examiner states that Yoshino et al. teach all the limitations of claims 13 and 14, except for the specific rate of administration of edaravone. The Ikeda reference is relied upon to *allegedly* remedy this deficiency. However, Ikeda fails to remedy the above discussed deficiency of the Yoshino et al. reference, specifically regarding the

dosing regimen. Accordingly, claims 13 and 14 are not rendered obvious by Yoshino et al. in view of Ikeda.

For the reasons provided above, reconsideration and withdrawal of the obviousness rejections are respectfully requested.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

Hiide YOSHINO et al.

By /Amy E. Schmid/ Digitally signed by /Amy E. Schmid/ DN: cn=/Amy E. Schmid/, o, ou, email=aschmid@wenderoth.com, c=US Date: 2011.11.22 12:50:15 -05'00'

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November 22, 2011

Attachments:
(1) Declaration of Mr. Takatomo Yoneoka
(2) Neurology, "The ALSFRSr predicts survival time in an ALS clinic population", 2005, Vol. 64, pages 38-43